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#3	Search **Wu L 1997**	07:05:57	166
#2	Search **2D7 and LeukoSite, Inc.**	06:36:55	2

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=> "anti-CCR5"
        389022 "ANTI"
             9 "ANTIS"
        389029 "ANTI"
                 ("ANTI" OR "ANTIS")
          3804 "CCR5"
L1          98 "ANTI-CCR5"
                 ("ANTI"(W)"CCR5")

=> 2D7 (l) L1
            87 2D7
L2          11 2D7 (L) L1

=> D L2 IBIB ABS 1-11
```

L2 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1046453 CAPLUS
DOCUMENT NUMBER: 142:175004
TITLE: Soluble chemokine CCR5 receptor is present in human plasma
AUTHOR(S): Tsimanis, Alexander; Kalinkovich, Alexander; Bentwich, Zvi
CORPORATE SOURCE: R. Ben-Ari Institute of Clinical Imunology and AIDS Center, Kaplan Medical Center, Hebrew University Hadassah Medical School, Rehovot, Israel
SOURCE: Immunology Letters (2005), 96(1), 55-61
CODEN: IMLED6; ISSN: 0165-2478
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In view of the natural resistance to infection by HIV and occasional delayed clin. manifestation of the disease, as also the fact that the virus is able to enter only cells that express CD4 and a co-receptor, we initiated a search for a soluble co-receptor that might compete with its membrane counterpart. Using a sandwich ELISA system, a soluble human CCR5 receptor (sCCR5) was indeed detected in the circulation. Immunopptn. of sCCR5-pos. plasma samples from Israelis of Ethiopian and non-Ethiopian origin with mAb **2D7**, a conformation-dependent **anti-CCR5** antibody, revealed the presence of a .apprx.22 kDa protein. A panel of antibodies directed against the membrane receptor was used to characterize the structure of the soluble CCR5: mAb CTC8, recognizing the N-terminal sequence of the protein,10YDIN13; "multidomain" mAbs FAB181B and FAB183B that are dependent upon the presence of Q93 and D95 in ECL1 and K171 and E172 in ECL2A, and mAb FAB182B, recognizing the stretch 184YSQYQF189, which spans the C-terminal part of the second extracellular loop. The presence of short soluble CCR5 in human plasma has not been previously described. Among HIV-neg. non-Ethiopian Israelis, 20.4% were sCCR5-pos., as against only 10.5% in HIV-positives. However, 7.1% of HIV-neg. Ethiopian Israelis were sCCR5 pos., as were 5.6% HIV-positives. Plasma concns. of MIP-1β, the CCR5 agonist, were twice as high in sCCR5-positives (140.8 ± 25.8 pg/mL) as in the sCCR5-negatives (77.6

± 11.0 pg/mL, P = 0.0157). A significant pos. correlation between plasma levels of sCCR5 and MIP-1β was found (Fig. 4, r = 0.8, P < 0.0001).
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:900264 CAPLUS
DOCUMENT NUMBER: 140:92158
TITLE: Establishment of an HIV cell-cell fusion assay by using two genetically modified HeLa cell lines and reporter gene
AUTHOR(S): Sakamoto, Tatsunori; Ushijima, Hiroshi; Okitsu, Shoko; Suzuki, Eiko; Sakai, Koji; Morikawa, Shigeru; Muller, Werner E. G.
CORPORATE SOURCE: Graduate School of Medicine, Department of Developmental Medical Sciences, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan
SOURCE: Journal of Virological Methods (2003), 114(2), 159-166
CODEN: JVMEDH; ISSN: 0166-0934
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Infection of human cells with the human immunodeficiency virus type I (HIV-1) can be mimicked by a fusion process between cells expressing the HIV envelope protein (Env) and cells expressing both human CD4 together with the appropriate human chemokine receptors. In this study, a T-tropic HIV cell-cell fusion assay was established that utilized CD4, human CXCR4 and HIV NL4-3 gp160 as fusion components and a T7 polymerase-activated luciferase as a reporter system. The HeLa T4 cells used, expressed CD4 and CXCR4, and the applied HeLa KS386 cells expressed HIV NL4-3 gp160. By combining HeLa T4 cells with HeLa KS386 cells, an approx. about 100- to 300-fold increase in luciferase activity could be elicited relative to the control. The addition of anti-CD4 monoclonal antibody (Mab) (RPA-T4) or anti-CXCR4 Mab (12G5) in the assay significantly inhibited the fusion event; in contrast, an **anti-CCR5** Mab (**2D7**) had no effect, indicating that the fusion assay was CD4 and CXCR4 dependent. In this report, fusion events could be monitored by both the luciferase reporter system and syncytia formation. Fusion events were monitored and compared using these two approaches. The luciferase reporter system was found to be more sensitive than syncytia formation. Moreover, compared with previous HIV fusion models, such as using recombinant vaccinia viruses, this system has several advantages, including simplicity and sensitivity. Finally, the system provides a powerful tool to study fusion mechanisms mediated by T-tropic HIV gp160, as well as to screen for fusion-blocking antibodies and antiviral agents.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:645176 CAPLUS
DOCUMENT NUMBER: 135:343097
TITLE: Adaptation to Blockade of Human Immunodeficiency Virus Type 1 Entry Imposed by the **Anti-CCR5** Monoclonal Antibody **2D7**
AUTHOR(S): Aarons, Emma J.; Beddows, Simon; Willingham, Tim; Wu, Lijun; Koup, Richard A.
CORPORATE SOURCE: Department of Medicine, Division of Infectious Disease, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA
SOURCE: Virology (2001), 287(2), 382-390
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The second extracellular loop (ECL2) domain of CC-chemokine receptor 5 (CCR5) has been proposed as a specific target site for therapeutic agents aimed at blocking CCR5-dependent entry by human immunodeficiency virus type I (HIV-1). We have adapted two CCR5-using HIV-1 isolates, prototypic

JR-CSF, and a primary isolate, 11-121, to replicate in vitro in the presence of high concns. of a monoclonal antibody (MAb 2D7) specific for the CCR5 ECL2 domain. The 75% inhibitory concns. (IC75) for the two 2D7-adapted isolates were approx. 100-fold higher than those for corresponding control isolates passaged without the MAb. Adapted isolates did not acquire the ability to use CXCR4, CCR3, or CCR1. Env clones derived from MAb 2D7-adapted JR-CSF showed several gp120 mutations that were not found in any of the control JR-CSF clones. The in vitro observations suggest that CCR5-using HIV-1 strains might also be able to adapt in vivo to evade an ECL2-blocking therapeutic agent. (c) 2001 Academic Press.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:399156 CAPLUS

DOCUMENT NUMBER: 135:179630

TITLE: Human α1-acid glycoprotein binds to CCR5 expressed on the plasma membrane of human primary macrophages

AUTHOR(S): Atemezem, Aurelie; Mbemba, Elisabeth; Vassy, Roger; Slimani, Hocine; Saffar, Line; Gattegno, Liliane

CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, JE 2138, Faculte de Medecine Leonard de Vinci, Universite Paris XIII, Bobigny, 93017, Fr.

SOURCE: Biochemical Journal (2001), 356(1), 121-128
CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have reported previously that human α1-acid glycoprotein (AGP) inhibits the infection of human monocyte-derived macrophages (MDM) by R5 HIV-1, and that a disulfide-bridged peptide mimicking the clade B HIV-1 gp120 consensus V3 domain (V3Cs) binds specifically to CCR5 (the major co-receptor of R5 HIV strains) on these cells. The present study demonstrates that AGP binds specifically to MDM at high- and low-affinity binding sites with Kd values of 16 nM and 4.9 μM resp. The fact that heat denaturation of AGP only partly inhibited this binding (43%) suggests that protein-protein interactions are involved, as well as AGP glycans which are resistant to heat denaturation. Mannan, but not dextran, is a significant inhibitor (52%) of this binding, and sequential exoglycosidase treatment of AGP, which exposes penultimate mannose residues, has a strong stimulatory effect (.apprx. 2.8-fold). Therefore AGP glycans (probably mannose residues) are involved, at least partly, in the binding of AGP to MDM. In addition, AGP inhibits the binding of V3Cs and macrophage inflammatory protein-1β (MIP-1β) to MDM. The **anti-CCR5** monoclonal antibody **2D7**, specific for the second extracellular loop of CCR5, also inhibited AGP binding (67%), whereas **anti-CCR5** antibodies specific for the C-terminus of CCR5 region had no effect. Native AGP, like V3Cs (but not heat-denatured AGP), binds to 46 and 33-36 kDa electroblotted AGP-bound MDM membrane ligands, characterized as CCR5 by their interactions with **anti-CCR5** antibodies and with MIP-1β. Therefore both AGP glycans and MDM CCR5 are involved in the binding of AGP to MDM. This suggests that the inhibitory effect of AGP on the infection of human primary macrophages by R5 HIV-1 may be related to specific binding of AGP to a macrophage membrane lectin or lectin-like component and to CCR5.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:185460 CAPLUS

DOCUMENT NUMBER: 132:333214

TITLE: Inhibition of M-tropic HIV-1 infection by the fd phage-gene 3 protein with MIP-1α-binding activity

AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa

CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering,

Kagoshima University, Kagoshima, 890-0063, Japan
SOURCE: Molecular Immunology (2000), Volume Date 1999, 36(18), 1249-1254
CODEN: MOIMD5; ISSN: 0161-5890
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is a chemokine receptor with seven transmembrane-domains. It is expressed on T cells and macrophages and functions as the principal co-receptor for macrophage (M)-tropic strains of HIV-1. The **anti-CCR5** monoclonal antibody (mAb) **2D7** inhibits the binding and chemotaxis of the three natural β-chemokine ligands of CCR5, macrophage inflammatory protein (MIP)-1α, MIP-1β, and RANTES, to CCR5+ cells. The mAb also efficiently blocks the infectivity of several M-tropic and dual-tropic HIV-1 strains in vitro. In this study, the authors attempted to determine the peptide motif recognized with the **2D7** mAb. The authors isolated phage clones by panning a phage display library using **2D7** and identified three peptide motifs. One of these phage clones (M23) showed a marked inhibitory activity on HIV-1 infection. The unique sequence of 15 amino acids with an internal disulfide bond was inserted in the g3p of the M23 phage clone (M23-g3p). The M23-g3p was purified by fast-performance liquid chromatog. (FPLC). The authors show here that (1) M23-g3p was specifically recognized with **anti-CCR5** mAb; (2) M23-g3p showed inhibitory activity on the infectivity of M-tropic but not T-tropic HIV-1 strains; (3) M23-g3p bound to MIP-1α, MIP-1β, and RANTES but not MCP-1. These results suggested that the M23-g3p might mimic the CCR5-binding domain shared by β-chemokines, MIP-1α, MIP-1β, and RANTES as well as the HIV-1 infection.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:727861 CAPLUS
DOCUMENT NUMBER: 132:77404
TITLE: Relationship between Productive HIV-1 Infection of Macrophages and CCR5 Utilization
AUTHOR(S): Hung, Chia-Suei; Pontow, Suzanne; Ratner, Lee
CORPORATE SOURCE: Departments of Medicine, Pathology, Molecular Microbiology, Washington University School of Medicine, St. Louis, MO, 63110, USA
SOURCE: Virology (1999), 264(2), 278-288
CODEN: VIRLAX; ISSN: 0042-6822
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB HIV-1 isolates exhibit specificity for infection of immortalized T-cell lines and macrophages. The distinct cellular tropisms have been attributed to expression of coreceptors CXCR4 or CCR5, resp. However, it is unclear whether or not other tissue-specific determinants regulate entry. The current study uses a panel of viruses to analyze the relationship between CCR5 utilization and macrophage infection. Only chimeric viruses with the entire V3 loop from macrophage-tropic isolates, ADA or SF162, were able to infect macrophages. In contrast, chimeric viruses with smaller portions of the ADA V3 loop or the V3 loop of SF2, sufficient to allow CCR5 use, were insufficient for macrophage infection. PCR anal. showed that the defect in macrophage infection of the latter viruses was due to a defect in entry. Moreover, strains capable of infecting macrophages showed relative resistance to neutralization by **anti-CCR5** antibody, **2D7**, compared to strains which utilize CCR5 but are incapable of macrophage infection. (c) 1999 Academic Press.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:651420 CAPLUS
DOCUMENT NUMBER: 131:335588
TITLE: Enhanced expression, native purification, and

characterization of CCR5, a principal HIV-1 coreceptor
AUTHOR(S): Mirzabekov, Tajib; Bannert, Norbert; Farzan, Michael; Hofmann, Wolfgang; Kolchinsky, Peter; Wu, Lijun; Wyatt, Richard; Sodroski, Joseph
CORPORATE SOURCE: Department of Cancer Immunology and AIDS, Dana-Farber Cancer Institute, the Department of Pathology, Harvard Medical School, Harvard School of Public Health, Boston, MA, 02115, USA
SOURCE: Journal of Biological Chemistry (1999), 274(40), 28745-28750
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seven-transmembrane segment, G protein-coupled receptors (GPCRs) play important roles in many biol. processes in which pharmaceutical intervention may be useful. High level expression and native purification of GPCRs are important steps in the biochem. and structural characterization of these mols. Here, we describe enhanced mammalian cell expression and purification of a codon-optimized variant of the chemokine receptor CCR5, a GPCR that plays a central role in the entry of the human immunodeficiency virus-1 (HIV-1) into immune cells. CCR5 could be solubilized in its native state as determined by its ability to be precipitated by **2D7**, a conformation-dependent **anti-CCR5** antibody, and by the HIV-1 gp 120 envelope glycoprotein. The **2D7** antibody recognized immature and mature forms of CCR5 equally, whereas gp 120 preferentially recognized the mature form, a result that underscores a role for posttranslational modification of CCR5 in its HIV-1 coreceptor function. The methods described herein contribute to the anal. of CCR5 and are likely to be applicable to many other GPCRs.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:353334 CAPLUS
DOCUMENT NUMBER: 131:169077
TITLE: Peptide-motif analysis of phage clones selected by **anti-CCR5** monoclonal antibody (**2D7**)
AUTHOR(S): Meta, Akihiro; Torigoe, Naohiko; Ito, Yuji; Arakaki, Rieko; Nakashima, Hideki; Sugimura, Kazuhisa
CORPORATE SOURCE: Department of Bioengineering, Faculty of Engineering, Kagoshima University, Kagoshima, 890-0065, Japan
SOURCE: Peptide Science (1999), Volume Date 1998, 35th, 489-492
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Protein Research Foundation
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CCR5 is a chemokine receptor expressed on T cells and macrophages, and functions as the principal coreceptor for macrophage (M)-tropic HIV-1 strains. An **anti-CCR5** monoclonal antibody termed **2D7** completely blocks the binding and chemotaxis of the three natural chemokine ligands of CCR5, MIP-1α, MIP-1β and RANTES to CCR5+ cells. The **2D7** also efficiency blocks the infectivity of several M-tropic and dual-tropic HIV-1 strains in vitro. In this study, we attempted to determine the peptide motif recognized by **2D7**. By panning a phage display library by **2D7**, we isolated phage clones which were specifically recognized by **2D7** and characterized these motifs.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:263464 CAPLUS
DOCUMENT NUMBER: 131:57557
TITLE: Differential inhibition of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine

activity by monoclonal antibodies to CCR5
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most commonly transmitted human immunodeficiency virus type 1 (HIV-1) strains. The authors have isolated 6 new **anti-CCR5** murine monoclonal antibodies (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb **2D7** to specific amino acid residues in the N terminus and/or second extracellular loop regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) HIV-1 entry, (2) HIV-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit HIV-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited HIV-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and **2D7**, the most potent inhibitors of HIV-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting HIV-1 entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with **2D7**, RANTES, and CD4-IgG2, which inhibits HIV-1 attachment. The data support a model wherein HIV-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These antibodies will be useful for further dissecting these events.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:810699 CAPLUS
DOCUMENT NUMBER: 130:167066
TITLE: Microglia express CCR5, CXCR4, and CCR3, but of these, CCR5 is the principal coreceptor for human immunodeficiency virus type 1 dementia isolates
AUTHOR(S): Albright, Andrew V.; Shieh, Joseph T. C.; Itoh, Takayuki; Lee, Benhur; Pleasure, David; O'Connor, Michael J.; Doms, Robert W.; Gonzalez-Scarano, Francisco
CORPORATE SOURCE: Departments of Neurology and Microbiology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104-6146, USA
SOURCE: Journal of Virology (1999), 73(1), 205-213
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Microglia are the main human immunodeficiency virus (HIV) reservoir in the central nervous system and most likely play a major role in the development of HIV dementia (HIVD). To characterize human adult microglial chemokine receptors, the authors analyzed the expression and calcium signaling of CCR5, CCR3, and CXCR4 and their roles in HIV entry. Microglia expressed higher levels of CCR5 than of either CCR3 or CXCR4. Of these 3 chemokine receptors, only CCR5 and CXCR4 were able to transduce a signal in microglia in response to their resp. ligands, MIP-1β and SDF-1α, as recorded by single-cell calcium flux expts. The authors also found that CCR5 is the predominant coreceptor used for infection of

human adult microglia by the HIV type 1 dementia isolates HIV-1DS-br, HIV-1RC-br, and HIV-1YU-2, since the **anti-CCR5** antibody **2D7** was able to dramatically inhibit microglial infection by both wild-type and single-round luciferase pseudotype reporter viruses. Anti-CCR3 (7B11) and anti-CXCR4 (12G5) antibodies had little or no effect on infection. Last, the authors found that virus pseudotyped with the DS-br and RC-br envelopes can infect cells transfected with CD4 in conjunction with the G-protein-coupled receptors APJ, CCR8, and GPR15, which have been previously implicated in HIV entry.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:723554 CAPLUS
DOCUMENT NUMBER: 130:94276
TITLE: CCR5 has an expanded ligand-binding repertoire and is the primary receptor used by MCP-2 on activated T cells
AUTHOR(S): Ruffing, Nancy; Sullivan, Nancy; Sharmeen, Lamia; Sodroski, Joseph; Wu, Lijun
CORPORATE SOURCE: LeukoSite, Inc., Cambridge, MA, 02142, USA
SOURCE: Cellular Immunology (1998), 189(2), 160-168
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is a chemokine receptor expressed by T cells and macrophages, which also functions as the principal coreceptor for macrophage (M)-tropic HIV-1 strains to enter the host cells. Here, the authors aim to better understand the ligand-binding profiles of CCR5 and the chemokine-receptor usage on leukocytes. The authors found that MCP-2 could bind to CCR5 transfectants with high affinity and cross-compete effectively with RANTES, MIP-1α, and MIP-1β. MCP-2 is a true agonist for CCR5, eliciting a robust chemotactic response in CCR5 transfectants similar to that of the 3 known CCR5 ligands and exhibiting cross-desensitization with RANTES in the Ca2+ flux response. MCP-4 also bound to CCR5 with high affinity and was efficiently displaced by other CCR5 ligands. However, MCP-4 only partially displaced the binding of radiolabeled MIP-1α and caused a chemotactic response only at high concns. Furthermore, MCP-2 inhibited the binding of the M-tropic HIV-1 gp120 envelope glycoprotein to CCR5 and HIV-1 infection of peripheral blood mononuclear cells. More importantly, the authors found that MCP-2 could bind and elicit chemotaxis in CD3-activated and IL-2-maintained T cells, and most of these functions could be specifically inhibited by the **anti-CCR5** mAb **2D7**, whereas the responses mediated by MIP-1α or MCP-4 were only partially inhibited by **2D7**. Thus, although MCP-2 can bind to and signal through CCR1, CCR2b, and CCR5, among which both CCR2 and CCR5 are expressed at high levels on activated T cells, it appears to preferably utilize CCR5 on these cells. In contrast, MIP-1α and MCP-4 seem to activate multiple receptors on the same cells. (c) 1998 Academic Press.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> "second extracellular loop"
498679 "SECOND"
11548 "SECONDS"
509535 "SECOND"
("SECOND" OR "SECONDS")
165053 "EXTRACELLULAR"
116571 "LOOP"
42940 "LOOPS"
144964 "LOOP"
("LOOP" OR "LOOPS")
L3 400 "SECOND EXTRACELLULAR LOOP"
("SECOND"(W)"EXTRACELLULAR"(W)"LOOP")

=> L3 and L1

L4 9 L3 AND L1

=> antibody and L4
285626 ANTIBODY
333616 ANTIBODIES
448218 ANTIBODY
(ANTIBODY OR ANTIBODIES)
L5 9 ANTIBODY AND L4

=> D L5 IBIB ABS 1-9

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:575989 CAPLUS
DOCUMENT NUMBER: 143:304430
TITLE: Novel vaccine strategy against AIDS using cyclic dodecapeptide mimicking the loop structure of HIV-1 coreceptor, CCR5
AUTHOR(S): Misumi, Shogo; Takamune, Nobutoki; Shoji, Shozo
CORPORATE SOURCE: Department of Pharmaceutical Biochemistry, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, Kumamoto, 862-0973, Japan
SOURCE: Peptide Science (2005), Volume Date 2004, 41st, 343-346
CODEN: PSCIFQ; ISSN: 1344-7661
PUBLISHER: Japanese Peptide Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monoclonal **antibody** KB8C12, raised against a cyclic closed-chain dodecapeptide (cDDR5) mimicking the **second extracellular loop** (Arg168-Cys178) of CCR5, recognized naive CCR5 mols., and inhibited CCR5-mediated HIV-1 infection. Furthermore, antisera from cynomolgus monkeys immunized with the cDDR5 displayed anti-HIV-1 activities. These results suggest that cDDR5 is a useful immunogen to induce a conformation-dependent **anti-CCR5 antibodies** capable of blocking HIV-1 infection.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:456295 CAPLUS
DOCUMENT NUMBER: 143:24660
TITLE: Identification of a linear peptide recognized by monoclonal **antibody** 2D7 capable of generating CCR5-specific **antibodies** with human immunodeficiency virus-neutralizing activity
AUTHOR(S): Khurana, Surender; Kennedy, Michael; King, Lisa R.; Golding, Hana
CORPORATE SOURCE: Division of Viral Products, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (2005), 79(11), 6791-6800
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CCR5 is the major coreceptor for human immunodeficiency virus (HIV) infection. The murine monoclonal **antibody** (MAb) 2D7, which recognizes a conformation-dependent epitope in the **second extracellular loop** of CCR5, is one of the most potent inhibitors of R5 virus cell entry. However, attempts to humanize 2D7 for in vivo human use have been unsuccessful so far. A filamentous phage library expressing random peptides was used to identify a peptide mimotope that is recognized by MAb 2D7. A synthetic peptide containing this sequence (2D7-2SK) bound to MAb 2D7 with high affinity and reversed its HIV type 1 (HIV-1) fusion inhibitory activity. The peptide contains sequence homologies to two distal regions of the **second extracellular loop** of human CCR5, both of which are required for MAb 2D7 binding. Rabbit anti-2D7-mimotope **antibodies** competed with MAb 2D7 for binding to the 2D7-2SK peptide in Biacore

biosensor testing. Importantly, the rabbit anti-2D7-2SK **antibodies** bound to CCR5 on cells and specifically inhibited R5 (but not X4) envelope-mediated syncytium formation. These **antibodies** also neutralized infection of human peripheral blood mononuclear cells with R5 HIV isolates comparably to MAb 2D7. In summary, the authors have identified a novel peptide that closely mimics the MAb 2D7 epitope on CCR5. This peptide could be included as a potential vaccine candidate or to isolate 2D7-like human **antibodies** as entry inhibitors for R5 viruses.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:427593 CAPLUS
DOCUMENT NUMBER: 143:24658
TITLE: Natural **Antibodies** to CCR5 from Breast Milk Block Infection of Macrophages and Dendritic Cells with Primary R5-Tropic HIV-1
AUTHOR(S): Bouhlal, Hicham; Latry, Vanessa; Requena, Mary; Aubry, Sylvie; Kaveri, Srinivas V.; Kazatchkine, Michel D.; Belec, Laurent; Hocini, Hakim
CORPORATE SOURCE: Institut Nationale de la Sante et de la Recherche Medicale (INSERM) U743, Equipe d'Immunite et Biotherapies Muqueuses et Universite Rene Descartes Paris V, Institut Biomedical des Cordeliers, Paris, 75006, Fr.
SOURCE: Journal of Immunology (2005), 174(11), 7202-7209 CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the authors demonstrate that breast milk of 66% and 83% of HIV-seroneg. and seropos. women, resp., contains natural Abs of the secretory IgA and IgG isotypes directed against the CCR5 coreceptor for R5-tropic strains of HIV-1. Abs to CCR5 were affinity purified on a matrix to which a synthetic peptide corresponding to the **second extracellular loop** of CCR5 had been coupled. The purified Abs bound to the CCR5 peptide in a dose-dependent fashion and to both native CCR5 expressed by Chinese hamster ovary cells transfected with CCR5 gene, macrophages, and immature dendritic cells. Although the avidity differed, the amount of **anti-CCR5** Abs did not significantly differ between breast milk of HIV-seropos. and -seroneg. women. Purified **anti-CCR5** Abs inhibited up to 75% infection of macrophages and dendritic cells with HIVBaL and HIVJR-CSF. These observations provide evidence for a role of natural Abs to CCR5 in breast milk in controlling transmissibility of HIV through breast feeding.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1046453 CAPLUS
DOCUMENT NUMBER: 142:175004
TITLE: Soluble chemokine CCR5 receptor is present in human plasma
AUTHOR(S): Tsimanis, Alexander; Kalinkovich, Alexander; Bentwich, Zvi
CORPORATE SOURCE: R. Ben-Ari Institute of Clinical Imunology and AIDS Center, Kaplan Medical Center, Hebrew University Hadassah Medical School, Rehovot, Israel
SOURCE: Immunology Letters (2005), 96(1), 55-61 CODEN: IMLED6; ISSN: 0165-2478
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In view of the natural resistance to infection by HIV and occasional delayed clin. manifestation of the disease, as also the fact that the virus is able to enter only cells that express CD4 and a co-receptor, we initiated a search for a soluble co-receptor that might compete with its membrane counterpart. Using a sandwich ELISA system, a soluble human CCR5

receptor (sCCR5) was indeed detected in the circulation. Immunopptn. of sCCR5-pos. plasma samples from Israelis of Ethiopian and non-Ethiopian origin with mAb 2D7, a conformation-dependent **anti-CCR5 antibody**, revealed the presence of a .apprx.22 kDa protein. A panel of **antibodies** directed against the membrane receptor was used to characterize the structure of the soluble CCR5: mAb CTC8, recognizing the N-terminal sequence of the protein, 10YDIN13; "multidomain" mAbs FAB181B and FAB183B that are dependent upon the presence of Q93 and D95 in ECL1 and K171 and E172 in ECL2A, and mAb FAB182B, recognizing the stretch 184YSQYQF189, which spans the C-terminal part of the **second extracellular loop**. The presence of short soluble CCR5 in human plasma has not been previously described. Among HIV-neg. non-Ethiopian Israelis, 20.4% were sCCR5-pos., as against only 10.5% in HIV-positives. However, 7.1% of HIV-neg. Ethiopian Israelis were sCCR5 pos., as were 5.6% HIV-positives. Plasma concns. of MIP-1β, the CCR5 agonist, were twice as high in sCCR5-positives (140.8 ± 25.8 pg/mL) as in the sCCR5-negatives (77.6 ± 11.0 pg/mL, P = 0.0157). A significant pos. correlation between plasma levels of sCCR5 and MIP-1β was found (Fig. 4, r = 0.8, P < 0.0001).

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:318783 CAPLUS
DOCUMENT NUMBER: 139:173234
TITLE: Analysis of the mechanism by which the small-molecule CCR5 antagonists SCH-351125 and SCH-350581 inhibit human immunodeficiency virus type 1 entry
AUTHOR(S): Tsamis, Fotini; Gavrilov, Svetlana; Kajumo, Francis; Seibert, Christoph; Kuhmann, Shawn; Ketas, Tom; Trkola, Alexandra; Palani, Anadan; Clader, John W.; Tagat, Jayaram R.; McCombie, Stuart; Baroudy, Bahige; Moore, John P.; Sakmar, Thomas P.; Dragic, Tatjana
CORPORATE SOURCE: Microbiology and Immunology Department, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: Journal of Virology (2003), 77(9), 5201-5208
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human immunodeficiency virus type 1 (HIV-1) entry is mediated by the consecutive interaction of the envelope glycoprotein gp120 with CD4 and a coreceptor such as CCR5 or CXCR4. The CCR5 coreceptor is used by the most commonly transmitted HIV-1 strains that often persist throughout the course of infection. Compds. targeting CCR5-mediated entry are a novel class of drugs being developed to treat HIV-1 infection. In this study, we have identified the mechanism of action of two inhibitors of CCR5 function, SCH-350581 (AD101) and SCH-351125 (SCH-C). AD101 is more potent than SCH-C at inhibiting HIV-1 replication in primary lymphocytes, as well as viral entry and gp120 binding to cell lines. Both mols. also block the binding of several **anti-CCR5** monoclonal **antibodies** that recognize epitopes in the **second extracellular loop** of CCR5. Alanine mutagenesis of the transmembrane domain of CCR5 suggests that AD101 and SCH-C bind to overlapping but nonidentical sites within a putative ligand-binding cavity formed by transmembrane helixes 1, 2, 3, and 7. We propose that the binding of small mols. to the transmembrane domain of CCR5 may disrupt the conformation of its extracellular domain, thereby inhibiting ligand binding to CCR5.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:283870 CAPLUS
DOCUMENT NUMBER: 136:368158
TITLE: Multiple active states and oligomerization of CCR5 revealed by functional properties of monoclonal **antibodies**
AUTHOR(S): Blanpain, Cedric; Vanderwinden, Jean-Marie; Cihak,

Josef; Wittamer, Valerie; Le Poul, Emmanuel; Issafras, Hassan; Stangassinger, Manfred; Vassart, Gilbert; Marullo, Stefano; Schlondorff, Detlef; Parmentier, Marc; Mack, Matthias

CORPORATE SOURCE: Institut de Recherche Interdisciplinaire en Biologie Humaine et Nucleaire, Universite Libre de Bruxelles, Brussels, B-1070, Belg.

SOURCE: Molecular Biology of the Cell (2002), 13(2), 723-737
CODEN: MBCEEV; ISSN: 1059-1524

PUBLISHER: American Society for Cell Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CC-chemokine receptor 5 (CCR5) is the principal coreceptor for macrophage-tropic strains of human immunodeficiency virus type 1 (HIV-1). The authors have generated a set of **anti-CCR5** monoclonal **antibodies** and characterized them in terms of epitope recognition, competition with chemokine binding, receptor activation and trafficking, and coreceptor activity. MC-4, MC-5, and MC-7 mapped to the amino-terminal domain, MC-1 to the **second extracellular loop**, and MC-6 to a conformational epitope covering multiple extracellular domains. MC-1 and MC-6 inhibited regulated on activation normal T cell expressed and secreted (RANTES), macrophage inflammatory polypeptide-1β, and Env binding, whereas MC-5 inhibited macrophage inflammatory polypeptide-1β and Env but not RANTES binding. MC-6 induced signaling in different functional assays, suggesting that this monoclonal **antibody** stabilizes an active conformation of CCR5. Flow cytometry and real-time confocal microscopy showed that MC-1 promoted strong CCR5 endocytosis. MC-1 but not its monovalent isoforms induced an increase in the transfer of energy between CCR5 mols. Also, its monovalent isoforms bound efficiently, but did not internalize the receptor. In contrast, MC-4 did not prevent RANTES binding or subsequent signaling, but inhibited its ability to promote CCR5 internalization. These results suggest the existence of multiple active conformations of CCR5 and indicate that CCR5 oligomers are involved in an internalization process that is distinct from that induced by the receptor's agonists.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:645176 CAPLUS

DOCUMENT NUMBER: 135:343097

TITLE: Adaptation to Blockade of Human Immunodeficiency Virus Type 1 Entry Imposed by the **Anti-CCR5** Monoclonal **Antibody** 2D7

AUTHOR(S): Aarons, Emma J.; Beddows, Simon; Willingham, Tim; Wu, Lijun; Koup, Richard A.

CORPORATE SOURCE: Department of Medicine, Division of Infectious Disease, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA

SOURCE: Virology (2001), 287(2), 382-390
CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **second extracellular loop** (ECL2) domain of CC-chemokine receptor 5 (CCR5) has been proposed as a specific target site for therapeutic agents aimed at blocking CCR5-dependent entry by human immunodeficiency virus type I (HIV-1). We have adapted two CCR5-using HIV-1 isolates, prototypic JR-CSF, and a primary isolate, 11-121, to replicate in vitro in the presence of high concns. of a monoclonal **antibody** (MAb 2D7) specific for the CCR5 ECL2 domain. The 75% inhibitory concns. (IC75) for the two 2D7-adapted isolates were approx. 100-fold higher than those for corresponding control isolates passaged without the MAb. Adapted isolates did not acquire the ability to use CXCR4, CCR3, or CCR1. Env clones derived from MAb 2D7-adapted JR-CSF showed several gp120 mutations that were not found in any of the control JR-CSF clones. The in vitro observations suggest that CCR5-using HIV-1 strains might also be able to adapt in vivo to evade an ECL2-blocking therapeutic agent. (c) 2001 Academic Press.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:399156 CAPLUS
DOCUMENT NUMBER: 135:179630
TITLE: Human α1-acid glycoprotein binds to CCR5 expressed on the plasma membrane of human primary macrophages
AUTHOR(S): Atemezem, Aurelie; Mbemba, Elisabeth; Vassy, Roger; Slimani, Hocine; Saffar, Line; Gattegno, Liliane
CORPORATE SOURCE: Laboratoire de Biologie Cellulaire, JE 2138, Faculte de Medecine Leonard de Vinci, Universite Paris XIII, Bobigny, 93017, Fr.
SOURCE: Biochemical Journal (2001), 356(1), 121-128
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have reported previously that human α1-acid glycoprotein (AGP) inhibits the infection of human monocyte-derived macrophages (MDM) by R5 HIV-1, and that a disulfide-bridged peptide mimicking the clade B HIV-1 gp120 consensus V3 domain (V3Cs) binds specifically to CCR5 (the major co-receptor of R5 HIV strains) on these cells. The present study demonstrates that AGP binds specifically to MDM at high- and low-affinity binding sites with Kd values of 16 nM and 4.9 μM resp. The fact that heat denaturation of AGP only partly inhibited this binding (43%) suggests that protein-protein interactions are involved, as well as AGP glycans which are resistant to heat denaturation. Mannan, but not dextran, is a significant inhibitor (52%) of this binding, and sequential exoglycosidase treatment of AGP, which exposes penultimate mannose residues, has a strong stimulatory effect (.apprx. 2.8-fold). Therefore AGP glycans (probably mannose residues) are involved, at least partly, in the binding of AGP to MDM. In addition, AGP inhibits the binding of V3Cs and macrophage inflammatory protein-1β (MIP-1β) to MDM. The **anti-CCR5** monoclonal **antibody** 2D7, specific for the **second extracellular loop** of CCR5, also inhibited AGP binding (67%), whereas **anti-CCR5 antibodies** specific for the C-terminus of CCR5 region had no effect. Native AGP, like V3Cs (but not heat-denatured AGP), binds to 46 and 33-36 kDa electroblotted AGP-bound MDM membrane ligands, characterized as CCR5 by their interactions with **anti-CCR5 antibodies** and with MIP-1β. Therefore both AGP glycans and MDM CCR5 are involved in the binding of AGP to MDM. This suggests that the inhibitory effect of AGP on the infection of human primary macrophages by R5 HIV-1 may be related to specific binding of AGP to a macrophage membrane lectin or lectin-like component and to CCR5.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:263464 CAPLUS
DOCUMENT NUMBER: 131:57557
TITLE: Differential inhibition of human immunodeficiency virus type 1 fusion, gp120 binding, and CC-chemokine activity by monoclonal **antibodies** to CCR5
AUTHOR(S): Olson, William C.; Rabut, Gwenael E. E.; Nagashima, Kirsten A.; Tran, Diep N. H.; Anselma, Deborah J.; Monard, Simon P.; Segal, Jeremy P.; Thompson, Daniah A. D.; Kajumo, Francis; Guo, Yong; Moore, John P.; Maddon, Paul J.; Dragic, Tatjana
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY, 10016, USA
SOURCE: Journal of Virology (1999), 73(5), 4145-4155
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CC-chemokine receptor CCR5 mediates fusion and entry of the most

commonly transmitted human immunodeficiency virus type 1 (HIV-1) strains. The authors have isolated 6 new **anti-CCR5** murine monoclonal **antibodies** (MAbs), designated PA8, PA9, PA10, PA11, PA12, and PA14. A panel of CCR5 alanine point mutants was used to map the epitopes of these MAbs and the previously described MAb 2D7 to specific amino acid residues in the N terminus and/or **second extracellular loop** regions of CCR5. This structural information was correlated with the MAbs' abilities to inhibit (1) HIV-1 entry, (2) HIV-1 envelope glycoprotein-mediated membrane fusion, (3) gp120 binding to CCR5, and (4) CC-chemokine activity. Surprisingly, there was no correlation between the ability of a MAb to inhibit HIV-1 fusion-entry and its ability to inhibit either the binding of a gp120-soluble CD4 complex to CCR5 or CC-chemokine activity. MAbs PA9-PA12, whose epitopes include residues in the CCR5 N terminus, strongly inhibited gp120 binding but only moderately inhibited HIV-1 fusion and entry and had no effect on RANTES-induced calcium mobilization. MAbs PA14 and 2D7, the most potent inhibitors of HIV-1 entry and fusion, were less effective at inhibiting gp120 binding and were variably potent at inhibiting RANTES-induced signaling. With respect to inhibiting HIV-1 entry and fusion, PA12 but not PA14 was potently synergistic when used in combination with 2D7, RANTES, and CD4-IgG2, which inhibits HIV-1 attachment. The data support a model wherein HIV-1 entry occurs in 3 stages: receptor (CD4) binding, coreceptor (CCR5) binding, and coreceptor-mediated membrane fusion. These **antibodies** will be useful for further dissecting these events.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> "CC-CKR5"
        200943 "CC"
          1047 "CCS"
        201866 "CC"
                  ("CC" OR "CCS")
            28 "CKR5"
L6          18 "CC-CKR5"
                  ("CC"(W)"CKR5")

=> antibody and L6
        285626 ANTIBODY
        333616 ANTIBODIES
        448218 ANTIBODY
                  (ANTIBODY OR ANTIBODIES)
L7           5 ANTIBODY AND L6

=> D L7 IBIB ABS 1-5

L7   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:499783  CAPLUS
DOCUMENT NUMBER:          135:103329
TITLE:                    Methods of identifying G protein-coupled receptors
                          associated with the uptake of macrophage-trophic HIV,
                          and their use in diagnosis and treatment of AIDS
INVENTOR(S):              Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried;
                          Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S):       The Aaron Diamond Aids Research Center, USA; New York
                          University
SOURCE:                   U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 858,660,
                          abandoned.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 6258527            B1    20010710    US 1997-861105          19970521
     US 2003096221         A1    20030522    US 2000-734221          20001211
PRIORITY APPLN. INFO.:                       US 1996-17157P      P   19960520
                                             US 1996-20043P      P   19960619
                                             US 1997-858660      B2  19970519
                                             US 1997-861105      A1  19970521
AB   Entry of HIV-1 into target cells requires cell surface CD4 as well as
     addnl. host cell cofactors.  A cofactor required for infection with virus
     adapted for growth in transformed T cell lines was recently identified and
     named fusin.  Fusin, however, does not promote entry of macrophage-tropic
     viruses that are believed to be the key pathogenic strains in vivo.  It
     has now been determined that the principal cofactor for entry mediated by the
     envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is
     CC-CKR5, a receptor for the β-chemokines RANTES,
     MIP-1α, and MIP-1β.  The uptake of the virus may be blocked by
     ligands for the receptor or by preventing the receptor gene expression and
     in control of the synergism between infection by other viruses and the
     spread of HIV into other cell types.  Expts. with viruses pseudotyped with
     different env glycoproteins showed that uptake was dependent upon the
     presence of chemokine receptors with different serotypes of the virus
     showing different receptor requirements.  Methods of using chemokine
     receptor-deficient host cells as expression hosts to identify receptor
     requirements of clin. isolates of HIV-1 are described.
REFERENCE COUNT:          57    THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7   ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         1998:229024  CAPLUS
DOCUMENT NUMBER:          128:279581
TITLE:                    Cloning, sequence, and expression of a mouse genomic
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clone for the **CC-CKR5** receptor and construction of knockout mutations
INVENTOR(S): Bergsma, Derk J.; Brawner, Mary E.; Shabon, Usman
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 834564	A2	19980408	EP 1997-307823	19971003
EP 834564	A3	19980513		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6388055	B1	20020514	US 1996-724984	19961003
JP 10179180	A2	19980707	JP 1997-307784	19971003

PRIORITY APPLN. INFO.: US 1996-724984 A 19961003

AB Mouse chemokine receptor **CC-CKR5** polypeptides and DNA (RNA) encoding such mouse **CC-CKR5** and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such mouse **CC-CKR5** in the development of gene knockout mice for use as a model for human immunodeficiency virus.. Expression vectors carrying the **CC-CKR5** gene are constructed and expressed in human embryonic kidney 293 cells. **Antibodies** to **CC-CKR5** are also claimed.

L7 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:772659 CAPLUS
DOCUMENT NUMBER: 128:33766
TITLE: Methods of identifying G-coupled receptors associated with macrophage-trophic HIV, and diagnostic and therapeutic uses thereof
INVENTOR(S): Littman, Dan R.; Deng, Hongkui; Ellmeier, Wilfried; Landau, Nathaniel R.; Liu, Rong
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744055	A1	19971127	WO 1997-US8926	19970520
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5939320	A	19990817	US 1996-666020	19960619
AU 9731434	A1	19971209	AU 1997-31434	19970520

PRIORITY APPLN. INFO.: US 1996-17157P P 19960520
US 1996-650412 A 19960520
US 1996-666020 A 19960619
WO 1997-US8926 W 19970520

AB Entry of HIV-1 into target cells requires cell surface CD4 as well as addnl. host cell cofactors. A cofactor required for infection with virus adapted for growth in transformed T cell lines was recently identified and named fusin. Fusin, however, does not promote entry of macrophage-tropic viruses that are believed to be the key pathogenic strains in vivo. It has now been determined that the principal cofactor for entry mediated by the envelope glycoproteins of primary macrophage-tropic strains of HIV-1 is

CC-CKR5, a receptor for the β-chemokines RANTES, MIP-1α, and MIP-1β. The cofactor is useful for screening of drugs capable of modulating the production of a translocation promoting agent and capable of treating AIDS.

L7 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:459509 CAPLUS
DOCUMENT NUMBER: 127:173725
TITLE: Development of resistance of human immunodeficiency virus type 1 to dextran sulfate associated with the emergence of specific mutations in the envelope gp 120 glycoprotein
AUTHOR(S): Este, Jose A.; Schols, Dominique; De Vreese, Karen; Van Laethem, Kristel; Vandamme, Anne-Mieke; Desmyter, Jan; De Clercq, Erik
CORPORATE SOURCE: Rega Institute for Medical Research, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Molecular Pharmacology (1997), 52(1), 98-104
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyanionic compds. are known to inhibit the binding of human immunodeficiency virus (HIV) to CD4+ cells and the subsequent fusion step between the virus and cells. An HIV-1 strain resistant to dextran sulfate (DS) was selected by cultivation of HIV-1 (NL4-3)-infected MT-4 cells in the presence of DS Mr 5000. DS did not inhibit the binding of DS-resistant virus to MT-4 cells or syncytium formation between MOLT cells and HUT-78 cells persistently infected with the DS-resistant virus. In addition, a monoclonal **antibody** with specificity for the V3 loop of envelope gp120 glycoprotein did not recognize the DS-resistant HIV-1 gp120 V3 loop. The following mutations were found in the gp120 mol. of the DS-resistant HIV-1 strain but not in the wild-type strain: S114N in the V1 loop region; S134N in the V2 loop region; K269E, Q278H, and N293D in the V3 loop region; N323S in the C3 region; a deletion of 5 amino acids (Phe-Asn-Ser-Thr-Trp) at positions 364-368 in the V4 loop; and R3871 in the CD4 binding domain. These results suggest that (i) DS interacts with specific amino acid residues in the gp 120 mol., (ii) the virus is able to overcome the inhibitory effect of DS on viral infectivity, (iii) cross-resistance developed against those polyanionic compds. that are structurally related to DS, and (iv) the mol. determinants of HIV cell tropism, syncytium-inducing ability, coreceptor (fusin/**CC-CKR5**) utilization, and polyanion resistance seem to be located in the env genome of HIV and specifically in the V3 loop domain.

L7 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:433148 CAPLUS
DOCUMENT NUMBER: 125:112550
TITLE: Cell type-specific fusion cofactors determine human immunodeficiency virus type 1 tropism for T-cell lines versus primary macrophages
AUTHOR(S): Alkhatib, Ghalib; Broder, Christopher C.; Berger, Edward A.
CORPORATE SOURCE: Lab. Viral Dis., Natl. Inst. Allergy and Infectious Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1996), 70(8), 5487-5494
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Work in this laboratory previously demonstrated that the tropism of different human immunodeficiency type 1 isolates for infection of human CD4+ continuous cell lines (e.g., T-cell lines and HeLa-CD4 transformants) vs. primary macrophages is associated with parallel intrinsic fusogenic specificities of the corresponding envelope glycoproteins (Envs). For T-cell line-tropic isolates, it is well established that the target cell must also contain a human-specific fusion cofactor(s) whose identity is unknown. In this study, we tested the hypothesis that the Env fusion specificities underlying T-cell line vs. macrophage tropism are determined by

distinct cell type-specific fusion cofactors. We applied a recombinant vaccinia virus-based reporter gene assay for Env-CD4-mediated cell fusion; the LAV and Ba-L Envs served as prototypes for T-cell line-tropic and macrophage-tropic isolates, resp. We examined CD4+ promyelocytic and monocytic cell lines that are infectible by T-cell line-tropic isolates and become susceptible to macrophage-tropic strains only after treatment with differentiating agents. We observed parallel changes in fusion specificity: untreated cells supported fusion by the LAV but not the Ba-L Env, whereas cells treated with differentiating agents acquired fusion competence for Ba-L. These results suggest that in untreated cells, the block to infection by macrophage-tropic isolates is at the level of membrane fusion; furthermore, the differential regulation of fusion permissiveness for the two classes of Envs is consistent with the existence of distinct fusion cofactors. To test this notion directly, we conducted expts. with transient cell hybrids formed between CD4-expressing nonhuman cells (murine NIH 3T3) and different human cell types. Hybrids formed with HeLa cells supported fusion by the LAV Env but not by the Ba-L Env, whereas hybrids formed with primary macrophages showed the opposite specificity; hybrids formed between HeLa cells and macrophages supported fusion by both Envs. These results suggest the existence of cell type-specific fusion cofactors selective for each type of Env, rather than fusion inhibitors for discordant Env-cell combinations. Finally, analyses based on recombinant protein expression and **antibody** blocking did not support the proposals by others that the CD44 or CD26 antigens are involved directly in the entry of macrophage-tropic isolates.